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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/858,332	05/15/2001	Grigoriy S. Tchaga	CLON-056CIP	2176
41064	7590	05/06/2005	EXAMINER	
BOZICEVIC, FIELD & FRANCIS (BD BIOSCIENCES)			KERR, KATHLEEN M	
1900 UNIVERSITY AVENUE			ART UNIT	
SUITE 200			PAPER NUMBER	
EAST PALO ALTO, CA 94303			1652	

DATE MAILED: 05/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/858,332

Applicant(s)

TCHAGA ET AL.

Examiner

Kathleen M. Kerr

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 November 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-20, 26-28 and 30-47 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-20, 26-28 and 30-47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>Entrez Protein</u> . |

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-final rejection (mailed on May 19, 2004), Applicants filed a response and amendment received on August 19, 2004 and November 24, 2004. Said amendment cancelled Claim 29, amended Claims 15, 16, 30, and 31, and added new Claims 39-47. Thus, Claims 15-20, 26-28, and 30-47 are pending in the instant Office action and will be examined herein.

Priority

2. As previously noted, the instant application is granted the benefit of priority for the U.S. Application Nos. 60/101,867 and 09/404,017 filed on September 25, 1998 and September 23, 1999, respectively.

By virtue of Applicant's amendments, Claim 15 (n=6) is now supported in the provisional filed September 25, 1998. As noted previously, Claim 30 is also supported therein. New Claim 39 is, however, not supported and is afforded an earliest effective filing date of May 15, 2001, the filing date of the instant application.

Compliance with the Sequence Rules

3. By virtue of Applicant's amendment to the specification (paragraph 20), the 5-mer polypeptide now is disclosed with a SEQ ID NO to be in compliance with the sequence rules.

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4. A sequence listing containing 27 SEQ ID NOs was received in computer readable form (CRF) and paper copy on November 24, 2004; said sequence listing has been entered. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to **fully** comply with the requirements of 37 C.F.R. § 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

- a) In Claim 15, 2 12-residue peptides are disclosed without benefit of SEQ ID NOs.
- b) In Claim 30, 2 16-residue peptides are disclosed without benefit of SEQ ID NOs.
- c) In Claim 39, 14 peptides of varying length are disclosed without benefit of SEQ ID NOs.

The noted sequences are not in the sequence listing as filed, thus Applicants must provide (1) a substitute copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its entry into the specification, (3) a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID NO.

Withdrawn - Objections to the Specification

5. Previous objection to the Abstract is withdrawn by virtue of Applicant's amendment.

Maintained - Objections to the Specification

6. Previous objection to specification for inconsistencies between the sequence listing and the drawings is maintained in part. Figure 2 remains unclear. The amendment to Figure 2B has not been entered. Appropriate amendments to the drawings are by way of filing substitute sheets

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with changes sketched in red ink and filing instructions to replace the originally filed drawings with the amended sheets (see M.P.E.P. § 608.02(p)).

The Examiner has, however, considered the substitute drawing and finds it still confusing in how the sequences are labeled. The Examiner suggests using original Figure 2B and amending the brief description of the drawing to include SEQ ID NOs by virtue of nucleotide location, such as ---the peptide encoded by nucleotides 1921-1983 is SEQ ID NO:25---.

7. Previous objection to the specification for having a confusing reference in paragraph [0102], the reference to “U.S. RE 30,985” is maintained. Applicant’s have neither amended the specification nor presented arguments as to why the reference is clear as written. Clarification is required.

Withdrawn - Claim Rejections - 35 U.S.C. § 112

8. Previous rejection of Claim 16 under 35 U.S.C. § 112, second paragraph, is withdrawn by virtue of Applicant’s amendment.

9. Previous rejection of Claims 15-20 and 26-28 under 35 U.S.C. § 112, second paragraph, as being indefinite for the inclusion of SEQ ID NO:22 is withdrawn. However, the Examiner reiterated as noted above, the absence of a SEQ ID NO identifier in the instant claims renders them non-compliant with the sequence rules and not allowable for that reason.

New or Maintained - Claim Rejections - 35 U.S.C. § 112

10. Previous rejection of Claims 30-38 under 35 U.S.C. § 112, second paragraph, as being indefinite for the use of “NH₂-” and “-COOH” is maintained and amended herein to include

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Claims 15-20, 26-28 and 39-47. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant argues that the amendments have overcome this rejection; the Examiner disagrees.

In Claim 15, for example, “NH₂-(His-Asn)_n” is an equivalent peptide to “(His-Asn)_n-COOH” by virtue of peptide residue nomenclature wherein every residue has an NH₂ group and has a COOH group. Thus, the mere iteration of NH₂ or COOH, particularly in the absence of SEQ ID NOs, does not define the metal affinity peptides as N or C terminus peptides. In Claims 15, 30 and 39, open language is used to describe the peptides, and, therefore, their location with respect to the protein-of-interest must be clear. The Examiner suggests that language such as that found in Claim 16 be included in Claims 15, 30, and 39 to clearly claim that the encoded affinity peptides must be at the end of an open reading frame of a protein.

Maintained - Claim Rejections - 35 U.S.C. § 101

11. Previous rejection of Claims 15-20 and 26-28, and 30-38 under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter is maintained and amended herein to include Claims 39-47. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant argues that the amendments to clarify Claims 15, 30, and 39 so as to read only on polynucleotides encoding N and C-terminal tag polypeptides obviates the instant rejection. The Examiner disagrees. Firstly, Claims 15, 30, and 39 remain unclear as noted above. Secondly, the N or C-terminal nature of the peptides encoded by the claimed polynucleotides does not indicate the hand-of-man as required to overcome the instant rejection.

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As previously noted, "Claims 15 and 30, as written, do not sufficiently distinguish over polynucleotides as they naturally exist because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206, USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of "isolated" or "purified" provided that support in the specification can be cited. See M.P.E.P. § 2105."

Withdrawn - Claim Rejections - 35 U.S.C. § 102

12. Previous rejection of Claims 15-20 under 35 U.S.C. § 102(e) as being anticipated by Sato (USPAP 2003/0079237A1 filed June 7, 1999) is withdrawn by virtue of Applicant's amendment to Claim 15 so as to achieve an earliest effective filing date of September 25, 1998 for the instant claims. Thus, Sato is not longer prior art to these claims.

13. Previous rejection of Claims 15-19 and 26-28 under 35 U.S.C. § 102(b) as being anticipated by CLONTECHniques (PROTetTM 6xHN Bacterial Expression System. October, 1999. pages 23-24) is withdrawn by virtue of Applicant's amendment so as to achieve an earliest effective filing date of September 25, 1998 for the instant claims. Thus, Sato is not longer prior art to these claims.

New or Maintained - Claim Rejections - 35 U.S.C. § 102

14. Previous rejection of Claims 30-33 under 35 U.S.C. § 102(b) as being anticipated by Hirota *et al.* (see IDS) is maintained. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant argues that the sequence (formerly SEQ ID NO:1) must be at the N or C-terminus. The Examiner disagrees. As noted above, the inclusion of NH₂- and -COOH does not particularly indicate that the tag must be on the terminus. Moreover, internal sequence of SEQ ID NO:1 can be considered an amino terminus tag for the downstream sequence and can be considered a carboxy terminus tag for the upstream sequence, thus meeting the limitation of Claim 31.

15. Previous rejection of Claims 30-34 and 36-38 under 35 U.S.C. § 102(a) as being anticipated by CLONTECHniques (HATTM Protein Expression & Purification System. July, 1998) is maintained. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant argues that the declaration filed under 37 C.F.R. § 1.131 obviates the instant rejection; the Examiner disagrees.

The declaration filed on August 19, 2004 under 37 C.F.R. § 1.131 has been considered but is ineffective to overcome the CLONTECHniques (HATTM Protein Expression & Purification System. July, 1998) reference. The evidence submitted is insufficient to establish a conception of the invention prior to the effective date of the reference. While conception is the mental part of the inventive act, it must be capable of proof, such as by demonstrative evidence or by a complete disclosure to another. Conception is more than a vague idea of how to solve a problem. The requisite means themselves and their interaction must also be comprehended. See *Mergenthaler v. Scudder*, 1897 C.D. 724, 81 O.G. 1417 (D.C. Cir. 1897).

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The Clontech Invention Disclosure Form is not convincing evidence that Applicant had conceived of the invention prior to July 1998 because said Form does not teach the claimed invention. The Clontech Invention Disclosure Form provided describes a polyhistidine sequence from an N-terminal peptide stretch of lactate dehydrogenase from chicken muscle (*Gallus gallus*) encompassing 32 amino acid residues. No sequence is attached; however, a search of the Entrez protein database identifies 14 chicken LDH sequences. Four of these sequences (all identical to each other) have 6 histidine residues in the first 32 residues (also as described in the Form) (see Entrez Protein attachment) and, thus, can be considered the chicken sequence identified in the Form. The description in the Form clearly teaches residues 1-32 of the chicken LDH sequence as an affinity tag and **not** residues 6-21 of said sequence as is claimed. Thus, the Form does not provide evidence that SEQ ID NO:1 was conceived of prior to July, 1998.

16. Claims 39-44 are rejected under 35 U.S.C. § 102(e) as being anticipated by Sato (USPAP 2003/0079237A1 filed June 7, 1999). The instant claims are drawn to a polynucleotide encoding a peptide having the formula (His-Asn)₇ and related products. As noted above, the language of Claim 39 does not limit the scope to N or C-terminal peptides.

Sato teaches a nucleic acid molecule that encodes mouse p75NTR (NADE); the sequence of mouse NADE comprises an internal fragment: His-Asn-His-Asn-His-Asn (see Figure 1A). Sato also teaches vectors (see paragraph [0137]) and prokaryotic and eukaryotic host cells (see paragraph [0143]) of the mouse NADE DNA sequence.” The Examiner further notes that the internal sequence of (His-Asn)₃ can be considered an amino terminus tag for the downstream sequence and can be considered a carboxy terminus tag for the upstream sequence, thus meeting the limitation of Claim 40.

Summary of Pending Issues

17. The following is a summary of the issues pending in the instant application:
- a) Compliance with the sequence rules for Claims 15-20, 26-28, and 30-47.
 - b) Figure 2 stands objected to for being unclear in its description.
 - c) The specification stands objected to for having a confusing reference in paragraph [0102], the reference to "U.S. RE 30,985".
 - d) Claims 15-20, 26-28 and 30-47 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the use of "NH₂-" and "-COOH".
 - e) Claims 15-20, 26-28 and 30-47 stand rejected under 35 U.S.C. § 101.
 - f) Claims 30-33 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Hirota *et al.*
 - g) Claims 30-34 and 36-38 stand under 35 U.S.C. § 102(a) as being anticipated by CLONTECHniques (HATTM Protein Expression & Purification System. July, 1998).
 - h) Claims 39-44 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Sato (USPAP 2003/0079237A1 filed June 7, 1999).

Conclusion

18. Claims 15-20, 26-28 and 30-47 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

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will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931.

The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Kathleen M Kerr
Primary Examiner
Art Unit 1652

April 29, 2005